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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,596	03/01/2002	Mark G. Curric	SEPR-P01-051	7919

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EXAMINER	
SPIVACK, PHYLLIS G	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 10/15/2003

10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/087,596	Currie et al.
Examiner	**Art Unit**
Phyllis G. Spivack	1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 2, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above, claim(s) *4, 10-13, and 41-46* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3, 5-9, and 14-40* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *5, 6, 7*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicants' Response to the Restriction Requirement filed September 2, 2003, Paper No. 9, is acknowledged. Applicants have elected Group I drawn to a pharmaceutical preparation comprising a nefazodonoid and a serotonin reuptake inhibitor, and a method for its preparation, claims 1-40. As a single, disclosed species, Applicants have elected with traverse fluoxetine.

The traversal is on the grounds that the elected species is not representative of all the compounds encompassed by Group I.

Applicants' traversal has been carefully considered but is not found persuasive. Numerous, structurally unrelated, compounds are encompassed within the group "serotonin reuptake inhibitors". The search required for one composition with nefazodone and fluoxetine varies, for example, from that comprising sertraline or any other structurally different serotonin reuptake inhibitor. Distinctness is further evidenced by the different classification based on the different active ingredients. Moreover, as to the burden of the search, classification is merely one indication of the burdensome nature of the required search. The literature search of the large number of possible serotonin reuptake inhibitors claimed herein is not necessarily co-extensive and is a major factor in determining burden. Clearly different issues exist and the request for a single, disclosed species is still deemed proper and is adhered to.

Claims 1-46 are presented. The subject matter presently under consideration are those pharmaceutical preparations comprising a nefazodonoid and a fluoxetinoid in claims 1-40. Claims 4, 10-13, 41-46 are withdrawn from consideration by the Examiner, 37 C FR 1.142(b), as being drawn to non-elected inventions.

Three Information Disclosure Statements filed, respectively, September 11, 2002, January 21, 2003 and July 21, 2003, Paper Nos. 5-7, are acknowledged and have been reviewed.

The disclosure is objected to for the following informality: Claims 6 and 40 are substantial duplicates. Intended use confers no patentable weight to composition claims.

Appropriate correction is required.

Claims 7 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The recitations "preferably H or Me", within the definition of R_1, and "preferably O", within the definition of Y, render claim 7 indefinite. It is unclear whether or not claim limitations are intended.

Claim 39 lacks clarity in that Applicants have failed to define the invention properly with respect to the method for preparing the pharmaceutical preparation. By definition, a composition is a product of combining various ingredients. An unobvious or novel element in the preparation is absent.

Claims 1-3, 5, 7, 14-18 and 25-31 are rejected under 35 U.S.C. 112, first paragraph, as lacking a clear written description of the invention and of the manner and process of practicing it, in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the same, and, as not setting forth the best mode contemplated by the inventors to carry out the invention.

The claims are directed to a pharmaceutical preparation comprising a nefazodonoid and a serotonin reuptake inhibitor (SRI) and methods for treating a 5-HT receptor-mediated disorder in an animal. However, only the combination of nefazodone with the serotonin reuptake inhibitor fluoxetine is described. There is no disclosure concerning any 5-HT receptor-mediated disorders. One skilled in the art finds no guidance with respect to therapeutic applications. Claim 26 does not find support in the specification in the form of definitive treatments for pathological conditions. There is no showing that Applicants had possession of the claimed invention of therapeutic treatments comprising co-administering a nefazodonoid and a serotonin reuptake inhibitor - other than what is well known in the prior art. The present level of skill in the art of psychiatry would reasonably require a more detailed written description directed to the means of carrying out 5-HT receptor-mediated disorders and disclosure as to what disorders are contemplated.

Claims 26-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to methods for treating any 5-HT receptor-mediated disorder in an animal comprising co-administering a nefazodonoid and a serotonin reuptake inhibitor (SRI). However, only the combination of nefazodone with the serotonin reuptake inhibitor fluoxetine is described in the specification. There is no disclosure concerning any 5-HT receptor-mediated

disorders. Both nefazodonoids and fluoxetinoids are individually well established in the prior art as effective antidepressant agents.

Attention is directed to In re Wands, 8 USPQ2d 1400 where the court set forth factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to treatment of any 5-HT receptor-mediated disorder comprising co-administering a nefazodonoid and any serotonin reuptake inhibitor.

The relative skill of those in the art is generally that of a Ph.D or M.D.

Each particular 5-HT receptor-mediated disorder has its own specific characteristics and etiology. The unpredictability observed with single agent therapy is compounded when a combination of agents is employed. The broad recitation "treating a 5-HT receptor-mediated disorder" is inclusive of many conditions that presently have no established successful therapies.

It is clear the art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy.

The breadth of the claims

The claims are very broad and inclusive of any disorder of the 5-HT receptor.

The amount of direction or guidance provided and the presence or absence of working examples

There are no working examples directed to the combination of nefazodonoid and any serotonin reuptake inhibitor.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to which particular 5-HT reuptake inhibitor in combination with which particular nefazodonoid would be preferred for treatment of the many disorders of the 5-HT receptor that are encompassed in the language of claim 26. The skilled artisan would expect the interaction of a particular combination of drugs in the treatment of a particular disease state to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for each agent. The instant specification sets forth no such

understanding nor any criteria for extrapolating beyond the combination of nefazodone and fluoxetine. Even for the combination set forth, no direction is provided to treat any other condition beyond depression. Absent reasonable *a priori* expectations of success for using a particular chemotherapeutic combination to treat any particular 5-HT receptor disorder, one skilled in the psychiatry art would have to test extensively many combinations of agents to discover which particular disorder responds to that particular combination. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5-9 and 14-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fava, M., J. Clin. Psychiatry., in view of the web site, Mhi Ask the Expert - SSRIs and Nefazodone.

Fava teaches an augmentation strategy via the administration of nefazodone and selective serotonin reuptake inhibitors. See Table 1 on page 27, where an advantage of nefazodone is disclosed to be the management of SSRI-induced sexual dysfunction. Fava does not, in

particular, focus on the administration of fluoxetine. The secondary reference, however, teaches the combination of 50 mg of nefazodone with 5 mg of fluoxetine to treat refractory depression. One skilled in the psychiatry art would have been motivated to prepare a combination product of nefazodone and fluoxetine and to administer it to treat depression in view of the combined teachings. Such would have been obvious in the absence of evidence to the contrary because fluoxetine is well established in the art as causing sexual dysfunction during therapy. It would have been reasonable to expect a pharmaceutical preparation comprising a nefazodonoid and a fluoxetinoid to help manage the drug-induced sexual dysfunction that often results subsequent to fluoxetine therapy, as well as efficacy in the treatment of refractory depression. Further, it would have been reasonable to expect a reduction in side effects from combined treatment as a result of the more favorable side effect profile of nefazodone, the absence of sexual dysfunction associated with its administration and the option of administering a lower dosage of fluoxetine.

No claim is allowed.

Any inquiry concerning this communication should be directed to Phyllis Spivack at telephone number 703-308-4703.

October 14, 2003

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER